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# Hydrophilic diamine ligands for catalytic asymmetric hydrogenation of C=O bonds

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**Abstract**—Asymmetric hydrogenations of phenylglyoxylate methyl ester and of acetophenone with catalytic amounts of iridium complexes containing hydrophilic chiral $C_2$-symmetric diamine ligands is reported. E.e. values of up to 68% are observed for complete acetophenone hydrogenation in hydrophilic media. The use of such ligands allowed catalyst recovery without loss of activity and enantioselectivity in at least four hydrogenation cycles. 

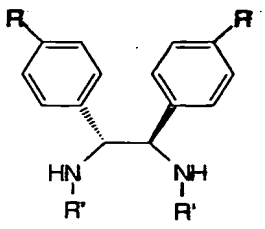
## 1. Introduction

Most of the catalysts used in homogeneous asymmetric hydrogenation reactions involve chiral bidentate phosphorus-containing ligands[1] which are often expensive and easily oxidized. However, various chiral nitrogen derivatives, such as $C_2$-symmetric diamines have been successfully used as chiral ligands in asymmetric transition metal-catalyzed reactions.[2] Our laboratory has developed a series of enantiomerically pure $C_2$-symmetric diamine and dithiourea ligands which are efficient catalysts for the hydrogenation of C=O and C=C bonds.[3,4] We have also shown that combining (1*R*,2*R*)-(+)-*N*,*N*′-dimethyl-1,2-diphenyl-ethylenediamine **2** with $[Ir(COD)_2]BF_4$ as catalyst precursor could induce high enantioselectivities in the hydrogenation of phenylglyoxylate methyl ester. From this point two areas of research are possible: on one hand new diamines could be synthesized in order to reach enantiomeric excess of practical interest (e.e. = 95%). On the other hand, the modification of known ligands, with a view to facilitating the separation and recycling of the catalysts, could be examined. For this last purpose, we present herein a means of introducing hydrophilic groups onto the diamine ligands (Scheme 1)

The synthesis of chiral diamines **3–5** is described and we also report the use of diamine ligands **1–5** in the presence of Rh, Ir and Ru precursors as chiral catalysts for the asymmetric hydrogenation of C=O bonds. In the case of hydrophilic systems containing diamines **3–5**, we describe the catalyst recovery studies.

## 2. Synthesis of hydrophilic enantiomerically pure diamines

(1*R*,2*R*)-(+)-1,2-Diphenyl-ethylenediamine **1** is commercially available. (1*R*,2*R*)-(+)-*N*,*N*′-Dimethyl-1,2-diphenyl-ethylenediamine **2** was prepared according to recently published procedures.[5] Ligand **3**, the methoxylated analog of diamine **2**, was prepared by coupling the corresponding imine as described by Alexakis and Mangeney,[5] with an improved yield of 98% of the (1:1) *d,l*-/*meso*-diamine mixture (Scheme 2). Resolution was not carried out on this crude mixture as reported because we noticed that several recrystallizations in ether led to a mixture enriched in *d,l* compound (*d,l*/*meso* = 75/25). Resolution was then possible with L-(+)-tartaric acid and (1*R*,2*R*)-(+)-*N*,*N*′-dimethyl-1,2-(4-methoxyphenyl)ethylenediamine **3** is obtained in more than 99.8% enantiomeric excess as determined by $^{31}P$ NMR. When $BBr_3$ was slowly added to a dichloromethane solution of the protected diamine **3** and further deprotection in acidic media was carried out (1*R*,2*R*)-(+)-*N*,*N*′-dimethyl-1,2-(4-hydroxyphenyl)-ethylenediamine **4** was obtained in 80% yield and 97%




**1**: R = H ; R' = H
**2**: R = H ; R' = $CH_3$
**3**: R = $OCH_3$ ; R' = $CH_3$
**4**: R = OH ; R' = $CH_3$
**5**: R = O-(-$C_2H_4O$-)$_3$-$CH_3$ ; R' = $CH_3$

Scheme 1. Chiral diamines used in hydrogenation reactions.

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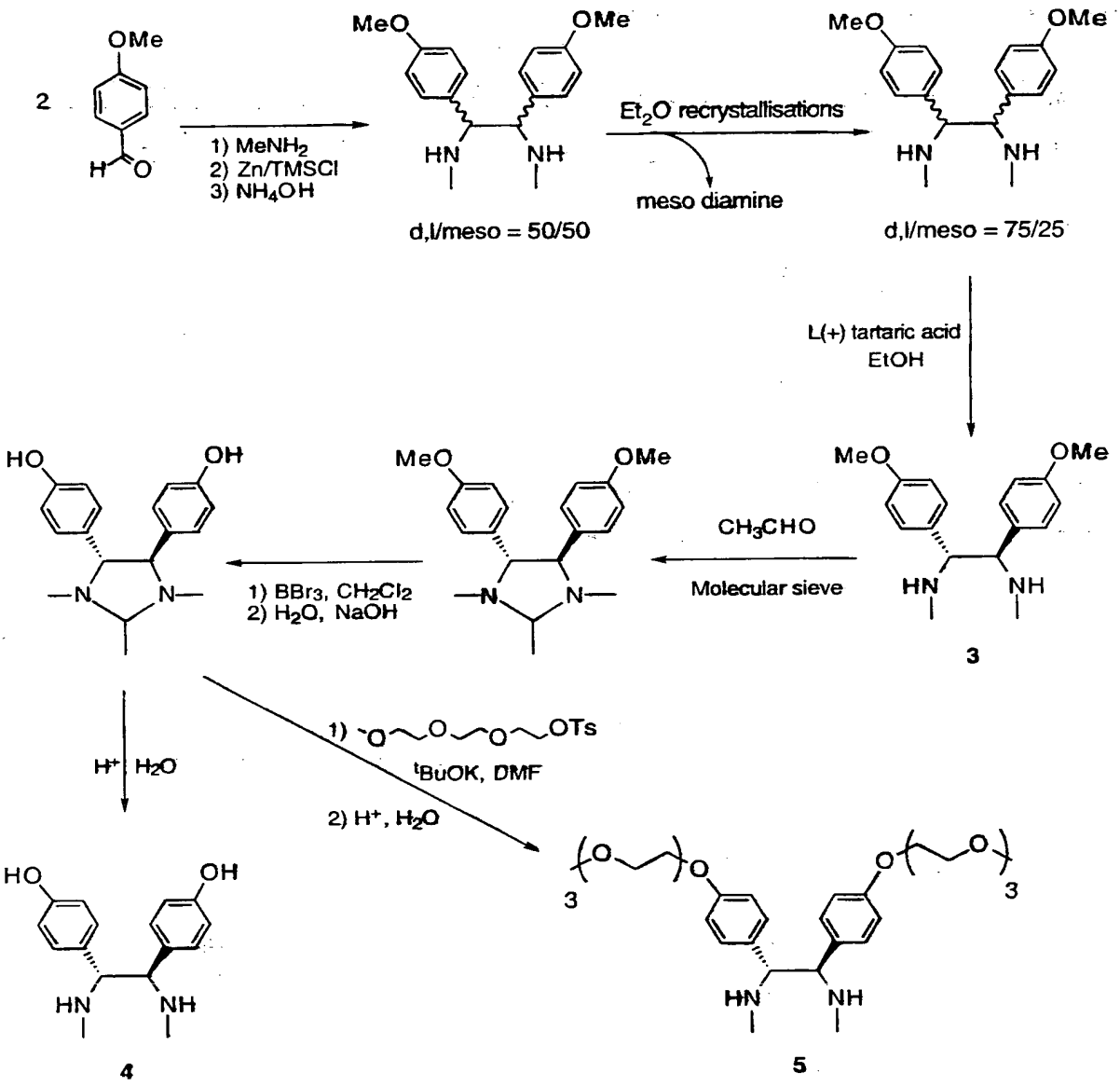



**Scheme 2.** Synthesis of diamines 3–5.

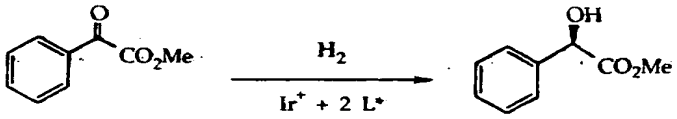
e.e. (1*R*,2*R*)-(+)-*N*,*N*′-Dimethyl-1,2-(4-methoxytriethylene glycol-phenyl)ethylenediamine **5** is prepared by *O*-alkylation of the protected diamine **4** in DMF at 110°C with tosylated triethylene glycol and further acid deprotection. The enantiomeric excess remains very high, with e.e. of 96%, but a moderate yield (33%) is obtained.

### 3. Asymmetric hydrogenation of phenylglyoxylate methyl ester

In previous work, Rh or Ir complexes of $C_2$-symmetric diamine **1** were used in the hydrogenation of phenylglyoxylate methyl ester.[3] As we then demonstrated that cationic species are more active than neutral ones, we used here $[Rh(NBD)_2]BF_4$ and $Ir[(COD)_2]BF_4$. For ruthenium, we employed the neutral complex, $[RuCOD(\eta^3\text{-}C_4H_7)_2]$. As for Ru and Rh catalysts, less than 30% e.e. was attained despite good activities, the results will not be described in detail. Chiral diamine **1**–**5** (2 equiv.) were added under an argon atmosphere to the iridium precursor in the chosen solvent. The solutions were used for the hydrogenation of phenylglyoxylate methyl ester. Results are summarized in Table 1.

We notice that (1*R*,2*R*)-(+)-1,2-diphenyl-ethylenediamine **1** gave the lowest e.e. values (entries 1 and 2). This may be due to the presence of two hydrogen atoms on the nitrogen binding site, thus avoiding the formation of stereogenic centres when the diamine is coordinated to iridium.[3] Diamines **1** and **2** led to better

**Table 1.** Diamines 1–5 as chiral inducers for phenylglyoxylate methyl ester hydrogenation




50 bars $H_2$; 50 °C; 15 hrs; [ketone] = 0.5 mol/L; 5% $[Ir(COD)_2]BF_4$

| Entry | L* | Solvent | % Yield | % E.e. (*R*) |
|---|---|---|---|---|
| 1 | 1 | THF | 99 | 31 |
| 2 | 1 | $H_2O$ | 100 | 15 |
| 3 | 2 | THF | 100 | 80 |
| 4 | 2 | $H_2O$ | 73 | 56 |
| 5 | 3 | THF | 100 | 45 |
| 6 | 3 | $H_2O$ | 96 | 50 |
| 7 | 4 | THF | 100 | 49 |
| 8 | 4 | $H_2O$ | 100 | 42 |
| 9 | 5 | THF | 98 | 43 |
| 10 | 5 | $H_2O$ | 100 | 54 |

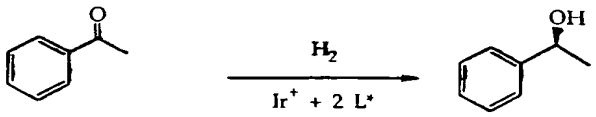
enantioselectivities when the corresponding iridium catalysts are formed in THF instead of water (entries 1 and 3 versus 2 and 4). A noticeable decrease in the catalytic activity is observed when using water as the solvent for ligand **2**. Conversely, the results in THF are similar to those obtained in water when ligands **3**, **4** and **5** are used: the presence of the hydroxy, methoxy and methoxytriethylene glycol groups on the diamine favours the solubility of the catalytic systems in water, which is one of the goals of our study. In addition, chiral induction of these hydrophilic ligands (entries 6, 8, and 10) is about the same as that observed for the diamine **2** in water (56%).

## 4. Asymmetric hydrogenation of acetophenone

We then extended our study to a more difficult substrate: acetophenone, which is a better model for practical synthetic applications. The hydrogenation reactions are carried out following the same experimental procedure as for phenylglyoxylate methyl ester using a substrate to catalyst molar ratio of 200 and 0.5% of $Ir[(COD)_2]BF_4$. The corresponding results are listed in Table 2.

As observed for phenylglyoxylate methyl ester, the reduction of acetophenone catalyzed by the iridium/diamine **2** complex in water gives lower activity and enantioselectivity than the reaction performed in THF (entries 1 and 2). Moderate conversions and enantiomeric excesses are obtained in THF with hydrophilic ligands **3**–**5** (entries 3, 5, and 7). When the same hydrogenations are carried out in water we notice a clear improvement of the catalytic activity but, except with diamine **5** the enantioselectivity diminishes (entries 7 and 8). Even though maximum asymmetric induction in water is only 48% with the hydrophilic diamines, this is clearly better than the result obtained with diamine **2** (27% e.e.).

**Table 2.** Diamines 2–5 as chiral inducers for acetophenone hydrogenation




50 bars $H_2$; 50 °C; 15 hrs; [ketone] = 0,6 mol/L; 0,5 % $[Ir(COD)_2]BF_4$

| Entry | L* | Solvent | % Yield | % E.e. (*R*) |
|---|---|---|---|---|
| 1 | 2 | THF | 71 | 63 |
| 2 | 2 | $H_2O$ | 49 | 27 |
| 3 | 3 | THF | 44 | 46 |
| 4 | 3 | $H_2O$ | 100 | 35 |
| 5 | 4 | THF | 50 | 61 |
| 6 | 4 | $H_2O$ | 82 | 24 |
| 7 | 5 | THF | 43 | 51 |
| 8 | 5 | $H_2O$ | 77 | 48 |

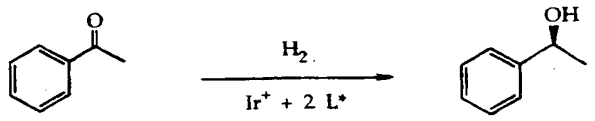
From both Tables 1 and 2, we notice that the introduction of the hydrophilic groups on the (1*R*,2*R*)-(+)-*N*,*N*′-dimethyl-1,2-diphenyl-ethylenediamine **2** allowed the use of water as solvent and improved both the activity and enantioselectivity of the corresponding iridium catalysts. This trend is clearer for the methoxytriethylene glycol diamine **5**. Despite this, the enantioselectivity of the aqueous catalysts (e.e. = 54%) still needs to be optimized.

## 5. Catalyst recovery tests

When (1*R*,2*R*)-(+)-*N*,*N*′-dimethyl-1,2-diphenyl-1,2-ethylenediamine **2** combined with $Ir[(COD)_2]BF_4$ is used as a catalyst for the hydrogenation of acetophenone, in water or a $H_2O$/MeOH mixture, low activity and enantioselectivity are observed, while iridium species containing hydrophilic diamines **3**–**5** induce 61–70% e.e. with complete conversion in methanol. The first attempts to recover the catalysts were thus carried out in a $H_2O$/MeOH (2/1) mixture. At the end of the hydrogenation run, pentane is added to the reaction mixture and two phases form: the organic layer is analyzed, while the aqueous phase containing the catalyst is replaced in the autoclave for reuse. A methanolic solution of acetophenone is then added to the catalyst solution in order to start the second hydrogenation cycle. Table 3 lists the results obtained with the hydrophilic diamines **3**–**5**.

In the first cycle, the three diamines **3**–**5** allowed complete acetophenone hydrogenation with similar enantioselectivities: 57–66% e.e. In the second cycle, the enantioselectivity was unchanged but the activity decreased so significantly that it dissuaded us to start further hydrogenation runs using the recycled catalyst.

**Table 3.** Diamines 3–5 as chiral inducers for acetophenone hydrogenation: catalyst recovery




50 bars $H_2$; 50 °C; 15 hrs; MeOH/$H_2O$; [ketone] = 0,6 mol/l.; 0,5 % $[Ir(COD)_2]BF_4$

| Entry | L* | Cycle | % Yield | % E.e. (*R*) |
|---|---|---|---|---|
| 1 | 3 | 1 | 100 | 63 |
| 2 | 3 | 2 | 69 | 57 |
| 3 | 4 | 1 | 100 | 66 |
| 4 | 4 | 2 | 70 | 62 |
| 5 | 5 | 1 | 100 | 58 |
| 6 | 5 | 2 | 43 | 54 |

Catalyst recovery can also be achieved using other hydrophilic solvents. Ethylene glycol and glycerol were introduced by Davies when studying the supported aqueous-phase catalysts (SAPCs).[6] This concept is based upon the immobilization of the catalytic species by means of the interaction of their hydrophilic ligands with a hydrophilic solid (glass, silica) in a thin film of a hydrophilic solvent (water, ethylene glycol). The organic substrates are commonly dissolved in a hydrophobic media and the reaction takes place at the interface of the two liquid phases.

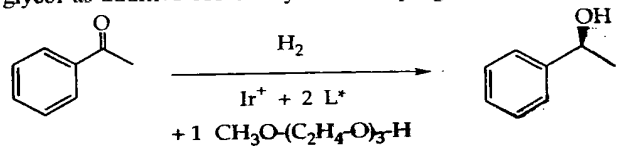
We studied the influence of methoxytriethylene glycol as additive in the catalyst recycling tests: the reactions are performed in the aqueous solvent ($H_2O$/MeOH) as previously described and methoxytriethylene glycol is added in a molar ratio of 1 with respect to the ligand. The reaction media are extracted with pentane after the test, so the aqueous phases could be reused for another hydrogenation cycle. The corresponding results are listed in Table 4.

The presence of methoxytriethylene glycol in the reactions using diamine **2** allowed us to recover the catalysts, which are sufficiently hydrophilic, in only 43% yield after the second run. In the case of diamines **3–5** we observe that the corresponding catalytic activities and enantioselectivities are preserved during the first four cycles when methoxytriethylene glycol is added. However, when increasing the methoxytriethylene glycol levels (entries 7 and 8), the catalytic activity decreased significantly in the fifth run. Thus, to get SAPC conditions we should increase the hydrophilicity of our ligands by adding longer polyethylene glycol chains.

## 6. Conclusion

Chiral diamine ligands have only been adapted recently for use in asymmetric hydrogenation reactions although they are more accessible than their phosphine counterparts. In the presence of chiral diamines, iridium can

**Table 4.** Methoxytriethylene glycol as additive for catalyst recovery agent




50 bars $H_2$; 50 °C; 15 hrs; MeOH/$H_2O$; [ketone] = 0,6 mol/l.; 0,5 % $[Ir(COD)_2]BF_4$

| Entry | L* | Cycle | % Yield | % E.e. (*R*) |
|---|---|---|---|---|
| 1 | 3 | 1–6 | 99–100 | 65–68 |
| 2 | 3 | 7 | 83 | 62 |
| 3 | 4 | 1–4 | 100 | 60–65 |
| 4 | 4 | 5 | 68 | 60 |
| 5 | 5 | 1–3 | 100 | 61–63 |
| 6 | 5 | 4 | 91 | 59 |
| 7 | 5[a] | 1–4 | 90–100 | 58–63 |
| 8 | 5[a] | 5 | 75 | 48 |

[a] Methoxytriethylene glycol/$H_2O$/MeOH = 1/2/1.

lead to higher enantioselectivities than the analogous rhodium or ruthenium species. We have also demonstrated that the diamines can be modified in order to obtain specific solubilities of the catalytic systems allowing their recovery in biphasic liquid media. The introduction of different hydrophilic groups onto (1*R*,2*R*)-(+)-*N*,*N*′-dimethyl-1,2-diphenyl-ethylenediamine **2** allowed the asymmetric hydrogenation of phenylglyoxylate methyl ester and of acetophenone in aqueous media. In the hydrogenation of acetophenone, catalyst recovery was possible for at least four hydrogenation cycles with complete conversions and unmodified enantioselectivities (up to 68%). This is encouraging because the chiral induction is about the same as that observed in THF and the yield is enhanced (71% yield and 63% e.e. in THF). We are now focusing on the SAPC applications of the iridium/ligand **5** complexes, notably by increasing the length of the polyethylene glycol groups on the ligand.

## 7. Experimental

### 7.1. General

Anhydrous THF (99.9% in a Sure/Seal™ bottle, Aldrich), EtOH (96%), MeOH, $CH_2Cl_2$, $Et_2O$ and pentane (Normapur) were used as received. Commercial methylamine, *p*-anisaldehyde, zinc dust, 1,2-dibromoethane, chlorotrimethylsilane, L-(+)-tartaric acid, DMF, tosylchloride, AcOEt, HCl, NaOH, NaCl, $NH_4Cl$, $NH_4OH$, AcOEt/$NEt_3$ and $PCl_3$ were used. $^1H$ and $^{13}C$ NMR spectra were recorded on a Bruker AC-200 Fourier-transform spectrometer and $\delta$ values are given in ppm (200.13 MHz for $^1H$ and 50.32 MHz for $^{13}C$). Optical rotations were measured with a Perkin–Elmer 241 polarimeter. Elemental analysis is carried out by the central analysis service of CNRS at Solaize.

### 7.2. Synthesis of diamines

(1*R*,2*R*)-(+)-1,2-Diphenyl-ethylenediamine **1** is commercially available from Fluka, $[\alpha]_D = +105$ (*c* 1, MeOH) and (1*R*,2*R*)-(+)-*N*,*N*′-dimethyl-1,2-diphenyl-ethylenediamine **2** was prepared according to recently published procedures.[5]

**7.2.1. (1*R*,2*R*)-(+)-*N*,*N*′-Dimethyl-1,2-(4-methoxyphenyl)ethylenediamine 3.** Zinc dust (<10 μm, 50 g, 0.76 mol) was suspended in anhydrous THF (200 mL), 1,2-dibromoethane (3 mL) was added as an activator under magnetic stirring. The mixture was heated under reflux for 1 min, cooled to room temperature before further 1,2-dibromoethane (6 mL) was added. A solution of 4-methoxybenzyl-*N*-methylimine (obtained by addition of aqueous methylamine to *p*-anisaldehyde, 112 g, 0.75 mol) in anhydrous THF, (400 mL) was added to the suspension. Chlorotrimethylsilane (200 mL, 1.58 mol) was added carefully over 30 min with a dropping funnel keeping the temperature below +40°C. The mixture was slowly heated to boiling temperature and heated under reflux for 4 h. The reaction mixture was cooled to −5°C before hydrolysis with 30% aqueous $NH_4OH$ (250 mL). Saturated aqueous $NH_4Cl$ (400 mL) was then added and the mixture stirred overnight at room temperature. After removal of the zinc dust by filtration through Celite, the liquid was extracted with $CH_2Cl_2$ (2×250 mL) and $Et_2O$ (2×250 mL). The combined organic layers were concentrated and 5 M HCl (400 mL) were added. The obtained aqueous layer was extracted with $Et_2O$ (2×250 mL) and basified with NaOH pellets. The organic layer was dried over $K_2CO_3$ and the solvent was removed to afford the crude product (98% yield). Two recrystallizations of the raw product from ether afforded a yellow solid which is a *d,l*/*meso* (75/25) mixture of the diamine **3** (73% yield). The resolution of 31.2 g of this mixture (containing 85.9 mmol of *d,l* diamine) was completed with L-(+)-tartaric acid (13.5 g, 90 mmol) in 96% ethanol. The precipitated salt was stirred with 2.5 M NaOH (300 mL) and the aqueous phase was extracted with $Et_2O$ (3×300 mL). The organic layer was dried on $K_2CO_3$ and the $Et_2O$ was removed to give a white solid. The enantiomeric excess was determined by formation of $PCl_3$ derivative, according to the published procedure.[5] After recrystallization in ether, 99.8% enantiomerically pure diamine **3** was isolated (5.86 g, 25% yield); mp 119.5°C; $[\alpha]_D = +35$ (*c* 1, $CHCl_3$); $^1H$ NMR ($CDCl_3$): 2.26 (2H, s, NH), 2.50 (6H, s, $CH_3$-NH), 3.50 (2H, s, *CH*-NH), 3.75 (6H, s, $CH_3$-O), 6.71 (4H, d, $J=8.7$ Hz, $C_{arom}H$, *meta*), 6.95 (4H, d, $J=8.7$ Hz, $C_{arom}H$, *ortho*); $^{13}C$ NMR ($CDCl_3$): 34.4 ($CH_3$-NH), 55.2 ($CH_3$-O), 70.3 (*CH*-NH), 113.4 ($C_{arom}H$, *meta*), 128.9 ($C_{arom}H$, *ortho*), 132.8 ($C_{arom}$-CH), 158.5 ($C_{arom}$-$OCH_3$, *para*). Anal. calcd for $C_{18}H_{24}N_2O_2$: C, 71.97; H, 8.05; N, 9.33; O, 10.65. Found: C, 71.83; H, 8.27; N, 9.34; O, 11.01%.

**7.2.2. (1*R*,2*R*)-(+)-*N*,*N*′-Dimethyl-1,2-(4-hydroxyphenyl)ethylenediamine 4.** Diamine **3** (4.3 g, 14.3 mmol) was poured into $Et_2O$ (70 ml) containing 4 Å molecular sieves (5 g) under magnetic stirring and acetaldehyde (1.5 mL, 26.6 mmol) was added. When the diamine was totally dissolved, the molecular sieves were removed by filtration. The ether and the excess acetaldehyde were also removed under vacuum to give the acetaminal quantitatively (98%). A solution of $BBr_3$ in $CH_2Cl_2$ (1 M, 54 mL) were slowly added to the a solution of the acetaminal (4.0 g, 12.2 mmol) in $CH_2Cl_2$ (50 mL) at −5°C. After stirring at room temperature for 20 h, the mixture was slowly hydrolyzed by treatment with 0.75 M NaOH (250 mL). After evaporating the $CH_2Cl_2$, the solution was filtered through Celite and the pH was adjusted to 8.5 with 0.1 M HCl: the precipitate was quantitatively (95%) recovered by filtration. The formed acetaminal is then cleaved with 2.5 M HCl (20 mL) and stirred for 30 min. $Et_2O$ (2 mL) were then added and stirring was continued for 30 min. The aqueous solution was then evaporated to a volume of 10 mL and the pH adjusted to 8.5 with 0.1 M NaOH to afford the solid diamine **4** recovered by filtration (2.92 g, 80%); mp 182°C; $[\alpha]_D = +102$ (*c* 1, DMSO); $^1H$ NMR (DMSO): 2.07 (6H, s, $CH_3$-NH), 3.27 (2H, s, *CH*-NH), 6.50 (4H, d, $J=8.3$ Hz, $C_{arom}H$, *ortho*), 6.79 (4H, d, $J=8.3$ Hz, $C_{arom}H$, *meta*); $^{13}C$ NMR (DMSO): 33.9

(*CH*$_3$-NH), 70.0 (*CH*-NH), 113.4 (*C*$_{arom}$*H*, *ortho*), 128.9 (*C*$_{arom}$*H*, *meta*), 131.7 (*C*$_{arom}$-CH-), 155.5 (*C*$_{arom}$*H*-OH, *para*). Anal. calcd for $C_{16}H_{20}N_2O_2$: C, 70.56; H, 7.40; N, 10.29; O, 11.75. Found: C, 70.62; H, 7.55; N, 10.08; O, 11.76%.

**7.2.3. (1*R*,2*R*)-(+)-*N*,*N*′-Dimethyl-1,2-(4-methoxytriethylene glycol-phenyl)ethylenediamine 5.** The protected diamine **3** (1 g, 3.35 mmol, prepared as for the synthesis of diamine **4**) was slowly stirred with 'BuOK (0.850 g, 7.57 mmol) for 15 min under an argon atmosphere. Anhydrous DMF (5 mL) was added and the mixture heated to 110°C before the addition of triethylene glycol tosylate derivative (3.2 g, 10.0 mmol). After 4 h when all the protected diamine was reacted (TLC control), AcOEt (20 mL) was added and the mixture cooled to room temperature. After filtration and evaporation of the solvent, the brown oil obtained was purified on silica gel column using AcOEt and AcOEt/$NEt_3$ (90/10) as eluant to separate the product of the remaining protected diamine. After removal of the solvent, a brown oil was obtained and stirred with HCl (1.11 mL, 13.4 mmol) in water (20 mL) during 30 min. This aqueous phase was saturated with NaCl and extracted with AcOEt (6×30 mL). The organic layer was dried over $K_2CO_3$ and the solvent was removed under vacuum to give pure diamine **5** (0.402 g, 21% yield); $[\alpha]_D = +67$ (*c* 1, $CDCl_3$); $^1$H NMR ($CDCl_3$): 2.18 (3H, s, *CH*$_3$-NH), 3.33 (3H, s, *CH*$_3$-O), 3.40 (1H, s, *CH*-NH), 3.50–4.00 (12H, m, O-*CH*$_2$-*CH*$_2$-O),), 6.73 (2H, d, $J=8.5$ Hz, *C*$_{arom}$*H*, *meta*), 6.86 (2H, d, $J=8.5$ Hz, *C*$_{arom}$*H*, *ortho*); $^{13}$C NMR ($CDCl_3$): 34.4 (*CH*$_3$-NH), 59.0 (*CH*$_3$-O), 69.9, 70.5, 70.6, 70.8, 70.9, 72.3 (O-*CH*$_2$*CH*$_2$-O), 77.4 (*CH*-NH), 114.0 (*C*$_{arom}$*H*, *meta*), 128.9 (*C*$_{arom}$*H*, *ortho*), 133.2 (*C*$_{arom}$-CH), 157.6 (*C*$_{arom}$-O, *para*). Anal. calcd for $C_{30}H_{48}N_2O_8$: C, 63.89; H, 8.57; N, 4.96; O, 22.67. Found: C, 63.98; H, 8.77; N, 4.49; O, 22.85%.

### 7.3. Catalytic hydrogenation of ketones

Acetophenone and phenylglyoxylate methyl ester (Aldrich) were used as received. Commercial catalyst precursors were used: $Ir[(COD)_2]BF_4$ and $[Rh(NBD)_2]BF_4$ from Strem and $[RuCOD(\eta^3\text{-}C_4H_7)_2]$ from Acros. When an argon atmosphere was required, Schlenk techniques were employed and solvents were degassed by argon bubbling for 30 min. Chiral gas chromatography analysis was carried out in a Shimadzu GC-14A chromatograph using a flame-ionization detector and a Shimadzu C-R6A integrator within a Lipodex A 25 m column.

**7.3.1. Typical hydrogenation procedure.** The metal precursor and the corresponding amount of chiral ligand were dissolved in the chosen solvent under an argon atmosphere at room temperature. After stirring for 30 min, the substrate was added and the resulting solution transferred to a purged stainless steel autoclave, containing a stirrer in a glass vessel. $H_2$ pressure is fixed to 50 bars and the autoclave heated to 50°C. After stirring overnight the autoclave is cooled and degassed. Solutions are filtered through Celite before CPV analysis.

**7.3.2. Catalyst recovery procedure.** After a first hydrogenation cycle carried out as described above, pentane (1 mL) is added to the reaction mixture. After shaking and short centrifuging, the organic phase was separated for CPV analysis while the aqueous phase was quickly replaced in the cleaned and purged autoclave with the corresponding amount of substrate solution. Hydrogen pressure and temperature are then fixed for the second hydrogenation run.

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